REMARKS

Claims 1, 3-7, 9-12, 14-17, 19, 20, and 34-45 are pending in the present application. Claims 34, 37, 40 and 43 have been canceled herein. Claims 1, 7, 12, and 17 have been amended herein; new claims 46-53 have been added herein. Thus, upon entry of the present amendment, claims 1, 3-7, 9-12, 14-17, 19, 20, 35, 36, 38, 39, 41, 42, and 44-53 will be under examination.

Regarding the amendments

Claims 1, 7, 12, and 17 have been amended to indicate that the ADP-glucose receptor polypeptide can be an amino acid sequence having at least 85% identity with SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose. These amendments are supported in the specification, for example, at page 28, line 28, to page 29, line 2.

New claims 46-48 depend from claim 3, which has been indicated to be allowable. New claims 46-48 are parallel to claims 4, 5, and 6, and are supported, for example, by claims 1 and 3-6 as originally filed.

New claims 49 and 50 depend from claim 9, which has been indicated to be allowable. New claims 49 and 50 are parallel to claims 10 and 11, and are supported, for example, by claims 7 and 9-11 as originally filed.

New claims 51 and 52 depend from claim 14, which has been indicated to be allowable. New claims 51 and 52 are parallel to claims 15 and 16, and are supported, for example, by claims 12 and 14-16 as originally filed.

New claim 53 depends from claim 19, which has been indicated to be allowable. New claim 53 is parallel to claim 20, and is supported, for example, by claims 17, 19 and 20 as originally filed.

As set forth above, the amendments and new claims are supported by the specification and do not add new matter. The claim amendments and new claims do not raise new issues for consideration or require a further search. Further, the amendments place the claims in better condition for allowance or for appeal. Accordingly, Applicants respectfully request that the Examiner enter the amendments and new claims.

Regarding the rejection under 35 U.S.C. § 112, first paragraph, enablement

The objection to the specification and corresponding rejection of claims 1, 4-7, 10-12, 15-17, 20 and 34-45 under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement in the specification, are respectfully traversed.

The Office Action alleges that the specification lacks sufficient guidance on modifying amino acid residues of SEQ ID NO:2 to allow one skilled in the art to make an ADP-glucose

receptor polypeptide having at least 85%, 95% or 99% identity with SEQ ID NO:2. Specifically, the Office Action alleges (a) that the specification fails to disclose the binding domains of ADP-glucose receptor SEQ ID NO:2 and residues of SEQ ID NO:2 critical for activity; (b) that the exhibits provided by Applicants in the response filed January 24, 2003, do not exemplify functional ADP-glucose receptors; and (c) that there are no working examples regarding how to make a functional ADP-glucose receptor modification having at least 85%, 95% or 99% identity with SEQ ID NO:2.

As amended, claims 1, 7, 12, and 17 recite an ADP-glucose receptor polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose. Applicants respectfully submit that the specification provides enablement for the full scope of these claims.

The Office Action alleges that the specification fails to disclose the binding domains of ADP-glucose receptor SEQ ID NO:2 and residues of SEQ ID NO:2 critical for activity. Applicants submit that the specification teaches binding domains and portions of SEQ ID NO:2 critical for activity, for example, by disclosing that modifications of residues within the second intracellular loop and the N and C segments of the third intracellular loop of SEQ ID NO:2 are predicted to be less well tolerated than modifications to other parts of the receptor (page 10, line 27, to page 11, line 7); and that residues in the transmembrane helices of SEQ ID NO:2 are predicted to be less

well tolerated than modifications to other parts of the receptor (page 10, lines 18-26). Using this guidance, those skilled in the art would have been able to make a variety of functional modifications of ADP-glucose receptor SEQ ID NO:2 having, for example, amino acid changes outside of the second intracellular loop, outside of the N and C segments of the third intracellular loop or outside of the transmembrane helices of SEQ ID NO:2, and would have expected that such modifications would retain activity. The activity of such modifications would have been readily confirmed by those skilled in the art using a variety of ADP-glucose receptor assays disclosed in the specification (see page 61, lines 12-30; page 62, lines 14-25; and page 35, line 16, to page 36, line 4). In view of these teachings in the specification, Applicants submit that one skilled in the art would have been able to prepare a functional ADP-glucose receptor polypeptide having at least 85% identity with SEQ ID NO:2 without undue experimentation.

The Office Action alleges that exhibits provided by Applicants in the response filed January 24, 2003, do not exemplify functional ADP-glucose receptors and states that Exhibit A shows a P2Y12 platelet ADP receptor, rather than an ADP-glucose receptor. Regarding the rat sequence having 86% identity with SEQ ID NO:2 (previously submitted in Exhibit A), Applicants submit that the name given to the sequence ("P2Y12 platelet ADP receptor") is not a definitive statement regarding polypeptide function. Similarly, lack of a specific functional name given to the macaque and mouse sequences having 97% and 88% identity with SEQ ID NO:2, respectively (previously submitted as

Exhibits B and C), is not a definitive statement regarding polypeptide function. Rather, Applicants have exemplified that the human ortholog of these sequences functions as an ADP-glucose receptor, a function not previously recognized for these receptors. Applicants submit that one skilled in the art, with the teachings in the specification that SEQ ID NO:2 corresponds to a functional human ADP-glucose receptor, and the disclosure of the nucleotide sequence of this receptor (SEQ ID NO:1) would have readily made a species ortholog having at least 85% identity with SEQ ID NO:2, such as those described above, using routine methods.

The Office Action argues that there are no working examples regarding how to make a functional ADP-glucose receptor modification having at least 85%, 95% or 99% identity with SEQ ID NO:2. Applicants submit that a working example is not required, and respectfully point out that the requirement is that the specification provide sufficient disclosure to teach those of ordinary skill how to make and use the invention as claimed. Applicants submit that the specification provides sufficient guidance to those skilled in the art for routinely preparing a functional ADP-glucose receptor having, for example, merely 4 amino acid changes with respect to SEQ ID NO:2, and to thereby obtain a modification having 99% identity with SEQ ID NO:2. Using this guidance, modifications of SEQ ID NO:2 having 95% or 85% identity with SEQ ID NO:2 similarly would have been routinely prepared by those skilled in the art. Undue experimentation would not have been required to make such a modification because the specification points out regions of SEQ ID NO:2 expected to

be intolerant of change that would have been used to select amino acid residues to be changed (see description herein above) and provides assays for confirming ADP-glucose receptor activity (see description herein above). In addition, laboratory procedures used for making such minor modifications were routine to those skilled in the art at the time of filing the present application. Therefore, Applicants respectfully submit that the specification provides sufficient guidance to enable methods for identifying an ADP-glucose receptor ligand, agonist or antagonist that employ an APD-glucose receptor having 85%, 95% or 99% identity with SEQ ID NO:2, such as species orthologs and other highly related ADP-glucose receptors capable of transducing a G-protein coupled signal in response to ADP-glucose.

The Office Action states that Applicants have argued that the portions of SEQ ID NO:2 critical for binding or functional activity of ADP-glucose receptor are unimportant with respect to naturally occurring modifications of SEQ ID NO:2. This is incorrect. Instead, Applicants argued that information regarding which portions of SEQ ID NO:2 are critical for binding or functional activity of the ADP-glucose receptor is unimportant for identifying species orthologs for ADP-glucose receptor using routine methods. In this regard, Applicants point out that a species ortholog for ADP-glucose receptor SEQ ID NO:2 would have been readily identified by one skilled in the art, for example, using any portion of the nucleotide sequence encoding SEQ ID NO:2 (SEQ ID NO:1) as a probe.

In view of the above remarks, Applicants respectfully request that the Examiner reconsider and remove the enablement rejection under the first paragraph of 35 U.S.C. § 112.

Regarding the rejection under 35 U.S.C. § 112, second paragraph

The rejection of claims 1, 4-7, 10-12, 15-17, and 20 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite is respectfully traversed. The Office Action states that these claims are indefinite for reciting "a minor modification of SEQ ID NO:2."

Applicants respectfully submit that the specification teaches that a "minor modification" of SEQ ID NO:2 refers to one or more additions, deletions or substitutions compared with the recited amino acid sequence; one or more chemical or enzymatic modifications to the polypeptide; or substitution of one or more L-configuration amino acids with corresponding D-configuration amino acids. Therefore, in light of the specification, those skilled in the art would have understood the metes and bounds of claims 1, 4-7, 10-12, 15-17, 20 as written. Nevertheless, claims 1, 7, 12, and 17 have been amended to recite an ADP-glucose receptor polypeptide comprising an amino acid sequence having at least 85% identity with SEQ ID NO:2 that transduces a G-protein coupled signal in response to ADP-glucose.

In view of the above, Applicants respectfully submit that claims 1, 4-7, 10-12, 15-17, and 20 are clear and definite. Accordingly, removal of this rejection under 35 U.S.C. § 112, second paragraph is requested.

CONCLUSION

In view of the amendments and the remarks submitted herein, Applicants submit that the claims are in condition for allowance and respectfully request a notice to that effect. The Examiner is invited to contact the undersigned agent or Cathryn Campbell if there are any questions relating to this application.

Respectfully submitted,

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Date

Pamela M. Guy
Registration No. 51,228
Telephone No. (858) 535-9001
Facsimile No. (858) 535-8949

McDERMOTT, WILL & EMERY
4370 La Jolla Village Drive
7th Floor
San Diego, California 92122